

CLAIMS

1. A herpes simplex virus (HSV) comprising:
 - 5 (i) an HSV LAT sequence inserted into an essential gene of the HSV;
and
 - (ii) a deletion in the endogenous LAT region of the HSV.
2. A virus according to claim 1 wherein the essential gene is an essential
10 immediate early (IE) gene.
3. A virus according to claim 2 wherein the essential IE gene is ICP27.
4. A virus according to claim 2 wherein the essential IE gene is ICP4.
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5. A virus according to any one of the preceding claims wherein the deletion
comprises at least some of the sequences present in the inserted HSV LAT sequence.
6. A virus according to any one of the preceding claims wherein the deletion
20 comprises at least 50% of the sequences present in the inserted LAT sequence.
7. A virus according to any one of the preceding claims wherein the deletion
comprises at least 75% of the sequences present in the inserted LAT sequence.
- 25 8. A virus according to any one of the preceding claims wherein the deletion
comprises at least all of the sequences present in the inserted LAT sequence.
9. A virus according to any one of the preceding claims wherein the LAT
sequence consists essentially of nucleotides 118866 to 120219 and/or nucleotides
30 117159 to 118865 of HSV1 strain 17+ (GenBank HE1CG), or the homologous
sequences of another HSV strain.
10. A virus according to any one of the preceding claims wherein the essential
gene comprises a deletion.
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11. A virus according to any one of the preceding claims which is selected from
an HSV1 strain, an HSV2 strain or derivatives thereof.

12. A virus according to claim 11 which is an HSV1 strain.
13. A virus according to any one of the preceding claims which carries at least one heterologous gene.
- 5 14. A virus according to claim 13 wherein said heterologous gene is operably linked to an/ the inserted HSV LAT sequence.
- 10 15. A virus according to claim 13 or 14 wherein said heterologous gene is operably linked to a control sequence permitting expression of said heterologous gene in mammalian cells.
16. A virus according to claim 15 wherein said mammalian cell is a cell of the central or peripheral nervous system of a mammal.
- 15 17. A virus according to claim 15 wherein said mammalian cell is a cell of the eye, heart or skeletal muscle of a mammal.
18. A virus according to any one of claims 13 to 17 wherein said heterologous gene encodes a polypeptide of therapeutic use.
- 20 19. A virus according to claim 18 wherein said gene encodes a polypeptide which is cytotoxic.
- 25 20. A virus according to claim 18 wherein said gene encodes a polypeptide capable of converting a precursor prodrug into a cytotoxic compound.
21. A virus according to any one of claims 15 to 18 wherein the heterologous gene is selected from genes encoding proteins involved in the regulation of cell division, enzymes involved in metabolic pathways, transcription factors and heat shock proteins.
- 30 22. A virus according to any one of claims 13 to 21 for use in delivering said heterologous gene to a mammalian cell.
- 35 23. A virus according to any one of claims 13 to 22 for use in a method of treatment of the human or animal body.

24. A virus according to claim 23 for use in the treatment of disorders of, or injuries to, the nervous system of a mammal.

25. Use of a herpes simplex virus according to any one of claims 13 to 22 in the manufacture of a medicament for use in the treatment of the human or animal body.

26. Use of a herpes simplex virus according to claim 25 in the treatment of disorders of, or injuries to, the nervous system of a mammal.

27. A pharmaceutical composition comprising an HSV strain according to any one of claims 13 to 22 together with a pharmaceutically acceptable carrier or diluent.

28. A method for studying the function of a heterologous gene in a mammalian cell which method comprises:

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(a) introducing said heterologous gene into a herpes simplex virus according to any one of claims 1 to 12;

(b) introducing the resulting herpes simplex virus into said mammalian cell; and

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(c) determining the effect of expression of said heterologous gene in said mammalian cell.

29. A method according to claim 28 wherein said heterologous gene is a wild-type or mutant gene implicated in causing disease.

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30. A method according to claim 28 or 29 wherein said mammalian cell is dysfunctional, said heterologous gene is wild-type and the effect of expression of said heterologous gene is determined by an assay for cellular function.

31. A method according to claim 28 or 29 wherein said mammalian cell has one or more endogenous genes inactivated by mutation.

32. A method for producing a herpes simplex virus according to claim 1, said method comprising:

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(i) inserted the HSV LAT sequence into an essential IE gene of the virus; and

(ii) deleting at least part of the LAT region of the virus.

33. A method of treating a disorder of, or injury to, the nervous system of a mammal comprising administering to a patient in need thereof an effective amount
5 of a virus according to any one of claims 10 to 19.